

PATENT COOPERATION TREATY

From the INTERNATIONAL SEARCHING AUTHORITY

To:
GLAXOSMITHKLINE
CIP (CN925.1)
Attn. Learoyd, Stephanie Anne
980 Great West Road
Brentford, Middlesex TW8 9GS
UNITED KINGDOM

15 AUG 2005

PCT
GlaxoSmithKline
Corporate IP
NOTIFICATION OF TRANSMITTAL OF
THE INTERNATIONAL SEARCH REPORT AND
THE WRITTEN OPINION OF THE INTERNATIONAL
SEARCHING AUTHORITY, OR THE DECLARATION
12 AUG 2005
ATT: SALE/SPD MT/SDP
SPM: N/A ON UPDATE Rule 44. 12/8/05
Date of mailing: 12/08/2005
Date of filing: 12/08/2005

Applicant's or agent's file reference SAL/PB60743	FOR FURTHER ACTION See paragraphs 1 and 4 below
International application No. PCT/EP2005/001540	International filing date (day/month/year) 10/02/2005
Applicant SMITHKLINE BEECHAM CORPORATION	

1. ☒ The applicant is hereby notified that the international search report and the written opinion of the International Searching Authority have been established and are transmitted herewith.

Filing of amendments and statement under Article 19:
The applicant is entitled, if he so wishes, to amend the claims of the International Application (see Rule 46):

When? The time limit for filing such amendments is normally 2 months from the date of transmittal of the International Search Report; however, for more details, see the notes on the accompanying sheet.

Where? Directly to the International Bureau of WIPO, 34 chemin des Colombettes
1211 Geneva 20, Switzerland, Facsimile No.: (41-22) 740.14.35

For more detailed instructions, see the notes on the accompanying sheet.

2. ☐ The applicant is hereby notified that no international search report will be established and that the declaration under Article 17(2)(a) to that effect and the written opinion of the International Searching Authority are transmitted herewith.

3. ☐ **With regard to the protest** against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:

☐ the protest together with the decision thereon has been transmitted to the International Bureau together with the applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices.

☐ no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.

4. **Reminders**


Shortly after the expiration of **18 months** from the priority date, the international application will be published by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau as provided in Rules 90bis.1 and 90bis.3, respectively, before the completion of the technical preparations for international publication.

The applicant may submit comments on an informal basis on the written opinion of the International Searching Authority to the International Bureau. The International Bureau will send a copy of such comments to all designated Offices unless an international preliminary examination report has been or is to be established. These comments would also be made available to the public but not before the expiration of 30 months from the priority date.

Within **19 months** from the priority date, but only in respect of some designated Offices, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase until **30 months** from the priority date (in some Offices even later); otherwise, the applicant must, **within 20 months** from the priority date, perform the prescribed acts for entry into the national phase before those designated Offices.

In respect of other designated Offices, the time limit of **30 months** (or later) will apply even if no demand is filed within 19 months.

See the Annex to Form PCT/IB/301 and, for details about the applicable time limits, Office by Office, see the *PCT Applicant's Guide*, Volume II, National Chapters and the WIPO Internet site.

Name and mailing address of the International Searching Authority  European Patent Office, P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Authorized officer Josef Ullrich
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NOTES TO FORM PCT/ISA/220

These Notes are intended to give the basic instructions concerning the filing of amendments under article 19. The Notes are based on the requirements of the Patent Cooperation Treaty, the Regulations and the Administrative Instructions under that Treaty. In case of discrepancy between these Notes and those requirements, the latter are applicable. For more detailed information, see also the PCT Applicant's Guide, a publication of WIPO.

In these Notes, "Article", "Rule", and "Section" refer to the provisions of the PCT, the PCT Regulations and the PCT Administrative Instructions respectively.

INSTRUCTIONS CONCERNING AMENDMENTS UNDER ARTICLE 19

The applicant has, after having received the international search report, one opportunity to amend the claims of the international application. It should however be emphasized that, since all parts of the international application (claims, description and drawings) may be amended during the international preliminary examination procedure, there is usually no need to file amendments of the claims under Article 19 except where, e.g. the applicant wants the latter to be published for the purposes of provisional protection or has another reason for amending the claims before international publication. Furthermore, it should be emphasized that provisional protection is available in some States only.

What parts of the international application may be amended?

Under Article 19, only the claims may be amended.

During the international phase, the claims may also be amended (or further amended) under Article 34 before the International Preliminary Examining Authority. The description and drawings may only be amended under Article 34 before the International Examining Authority.

Upon entry into the national phase, all parts of the international application may be amended under Article 28 or, where applicable, Article 41.

When?

Within 2 months from the date of transmittal of the international search report or 16 months from the priority date, whichever time limit expires later. It should be noted, however, that the amendments will be considered as having been received on time if they are received by the International Bureau after the expiration of the applicable time limit but before the completion of the technical preparations for international publication (Rule 46.1).

Where not to file the amendments?

The amendments may only be filed with the International Bureau and not with the receiving Office or the International Searching Authority (Rule 46.2).

Where a demand for international preliminary examination has been/is filed, see below.

How?

Either by cancelling one or more entire claims, by adding one or more new claims or by amending the text of one or more of the claims as filed.

A replacement sheet must be submitted for each sheet of the claims which, on account of an amendment or amendments, differs from the sheet originally filed.

All the claims appearing on a replacement sheet must be numbered in Arabic numerals. Where a claim is cancelled, no renumbering of the other claims is required. In all cases where claims are renumbered, they must be renumbered consecutively (Administrative Instructions, Section 205(b)).

The amendments must be made in the language in which the international application is to be published.

What documents must/may accompany the amendments?

Letter (Section 205(b)):

The amendments must be submitted with a letter.

The letter will not be published with the international application and the amended claims. It should not be confused with the "Statement under Article 19(1)" (see below, under "Statement under Article 19(1)").

The letter must be in English or French, at the choice of the applicant. However, if the language of the international application is English, the letter must be in English; if the language of the international application is French, the letter must be in French.

NOTES TO FORM PCT/ISA/220 (continued)

The letter must indicate the differences between the claims as filed and the claims as amended. It must, in particular, indicate, in connection with each claim appearing in the international application (it being understood that identical indications concerning several claims may be grouped), whether

- (i) the claim is unchanged;
- (ii) the claim is cancelled;
- (iii) the claim is new;
- (iv) the claim replaces one or more claims as filed;
- (v) the claim is the result of the division of a claim as filed.

The following examples illustrate the manner in which amendments must be explained in the accompanying letter:

1. [Where originally there were 48 claims and after amendment of some claims there are 51]:
"Claims 1 to 29, 31, 32, 34, 35, 37 to 48 replaced by amended claims bearing the same numbers; claims 30, 33 and 36 unchanged; new claims 49 to 51 added."
2. [Where originally there were 15 claims and after amendment of all claims there are 11]:
"Claims 1 to 15 replaced by amended claims 1 to 11."
3. [Where originally there were 14 claims and the amendments consist in cancelling some claims and in adding new claims]:
"Claims 1 to 6 and 14 unchanged; claims 7 to 13 cancelled; new claims 15, 16 and 17 added." or
"Claims 7 to 13 cancelled; new claims 15, 16 and 17 added; all other claims unchanged."
4. [Where various kinds of amendments are made]:
"Claims 1-10 unchanged; claims 11 to 13, 18 and 19 cancelled; claims 14, 15 and 16 replaced by amended claim 14; claim 17 subdivided into amended claims 15, 16 and 17; new claims 20 and 21 added."

"Statement under article 19(1)" (Rule 46.4)

The amendments may be accompanied by a statement explaining the amendments and indicating any impact that such amendments might have on the description and the drawings (which cannot be amended under Article 19(1)).

The statement will be published with the international application and the amended claims.

It must be in the language in which the international application is to be published.

It must be brief, not exceeding 500 words if in English or if translated into English.

It should not be confused with and does not replace the letter indicating the differences between the claims as filed and as amended. It must be filed on a separate sheet and must be identified as such by a heading, preferably by using the words "Statement under Article 19(1)."

It may not contain any disparaging comments on the international search report or the relevance of citations contained in that report. Reference to citations, relevant to a given claim, contained in the international search report may be made only in connection with an amendment of that claim.

Consequence if a demand for international preliminary examination has already been filed

If, at the time of filing any amendments under Article 19, a demand for international preliminary examination has already been submitted, the applicant must preferably, at the same time of filing the amendments with the International Bureau, also file a copy of such amendments with the International Preliminary Examining Authority (see Rule 62.2(a), first sentence).

Consequence with regard to translation of the international application for entry into the national phase

The applicant's attention is drawn to the fact that, where upon entry into the national phase, a translation of the claims as amended under Article 19 may have to be furnished to the designated/elected Offices, instead of, or in addition to, the translation of the claims as filed.

For further details on the requirements of each designated/elected Office, see Volume II of the PCT Applicant's Guide.

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference SAL/PB60743	FOR FURTHER ACTION see Form PCT/ISA/220 as well as, where applicable, item 5 below.	
International application No. PCT/EP2005/001540	International filing date (day/month/year) 10/02/2005	(Earliest) Priority Date (day/month/year) 12/02/2004
Applicant SMITHKLINE BEECHAM CORPORATION		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 7 sheets.



It is also accompanied by a copy of each prior art document cited in this report.

1. **Basis of the report**

- a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.



The international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

- b. ☐ With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, see Box No. I.

2. ☒ **Certain claims were found unsearchable** (See Box II).

3. ☐ **Unity of invention is lacking** (see Box III).

4. With regard to the **title**,



the text is approved as submitted by the applicant.



the text has been established by this Authority to read as follows:

BENZOFURAN AND BENZOTHIOPHENE DERIVATIVES USEFUL FOR THE TREATMENT OF CARDIOVASCULAR DISEASE

5. With regard to the **abstract**,



the text is approved as submitted by the applicant.



the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box No. IV. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. With regard to the **drawings**,

- a. the figure of the **drawings** to be published with the abstract is Figure No. _____



as suggested by the applicant.



as selected by this Authority, because the applicant failed to suggest a figure.



as selected by this Authority, because this figure better characterizes the invention.

- b. ☐ none of the figures is to be published with the abstract.

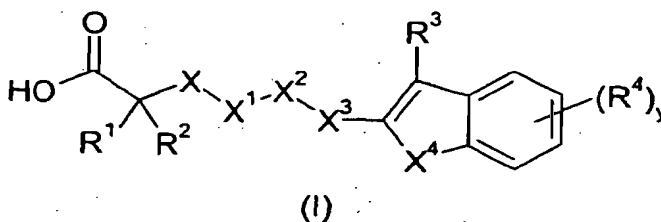
INTERNATIONAL SEARCH REPORT

International application No.

PCT/EP2005/001540

Box No. IV Text of the abstract (Continuation of item 5 of the first sheet)

A compound of formula (I) and pharmaceutically acceptable salts and solvates and hydrolysable esters thereof.



where X, X₁, X₂, X₃, X₄ and R, R₂, R₃, R₄ are defined as in claim I. These compounds are activators of the hPPAR receptors and are useful for the treatment of cardiovascular disease.

INTERNATIONAL SEARCH REPORT

International Application No
PCT/EP2005/001540

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07D333/54 C07D333/56 C07D417/12 C07D307/79 C07D307/80
A61K31/343 A61K31/381 A61K31/427 A61P3/06

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07D A61K A61P

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ, BEILSTEIN Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 97/28149 A (MERCK & CO.) 7 August 1997 (1997-08-07) cited in the application page 2, line 1 - page 4, line 26; claims; examples -----	1-21
A	US 5 859 051 A (ADAMS ET.AL.) 12 January 1999 (1999-01-12) cited in the application column 1, line 10 - column 3, line 15; claims; examples -----	1-21
A	EP 1 284 265 A (MITSUI CHEMICALS INC.) 19 February 2003 (2003-02-19) page 13, compounds 84 and 85 page 2, line 16 - page 3, line 18; claims; examples ----- -/--	1-21

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

° Special categories of cited documents :

A document defining the general state of the art which is not considered to be of particular relevance

E earlier document but published on or after the international filing date

L document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

O document referring to an oral disclosure, use, exhibition or other means

P document published prior to the international filing date but later than the priority date claimed

T later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

X document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

Y document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

& document member of the same patent family

Date of the actual completion of the international search

14 July 2005

Date of mailing of the international search report

12/08/2005

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Helps, I

INTERNATIONAL SEARCH REPORT

International Application No

PCT/EP2005/001540

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,A	WO 2004/037775 A (NOVO NORDISK) 6 May 2004 (2004-05-06) page 1, line 10 - page 3, line 5; claims; examples -----	1-21

INTERNATIONAL SEARCH REPORT

International application No.
PCT/EP2005/001540

Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.: 20, 21(PART)
because they relate to subject matter not required to be searched by this Authority, namely:
Although claims 20 and 21 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/EP2005/001540

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 9728149	A	07-08-1997	AT 245622 T	15-08-2003
			AU 1856997 A	22-08-1997
			AU 721452 B2	06-07-2000
			AU 2115997 A	22-08-1997
			CA 2245529 A1	07-08-1997
			DE 69723680 D1	28-08-2003
			DE 69723680 T2	15-04-2004
			EP 0888278 A1	07-01-1999
			ES 2202582 T3	01-04-2004
			JP 2002503202 T	29-01-2002
			WO 9728115 A1	07-08-1997
			WO 9728149 A1	07-08-1997
			AT 293963 T	15-05-2005
			AU 712607 B2	11-11-1999
			AU 1858197 A	22-08-1997
			CA 2244831 A1	07-08-1997
			DE 69733154 D1	02-06-2005
			EP 1011651 A1	28-06-2000
			JP 2000504021 T	04-04-2000
			WO 9727847 A1	07-08-1997
			AT 262334 T	15-04-2004
			AU 719146 B2	04-05-2000
			AU 2250797 A	22-08-1997
			CA 2245524 A1	07-08-1997
			DE 69728267 D1	29-04-2004
			DE 69728267 T2	24-02-2005
			EP 0904079 A1	31-03-1999
			ES 2217392 T3	01-11-2004
			JP 2002515865 T	28-05-2002
			WO 9727857 A1	07-08-1997
			AT 236137 T	15-04-2003
			AU 708055 B2	29-07-1999
			AU 1856397 A	22-08-1997
			CA 2244836 A1	07-08-1997
			DE 69720429 D1	08-05-2003
			DE 69720429 T2	15-01-2004
			EP 0882029 A1	09-12-1998
			ES 2194179 T3	16-11-2003
			JP 2002503203 T	29-01-2002
			WO 9728137 A1	07-08-1997
			US 5859051 A	12-01-1999
			US 6090836 A	18-07-2000
			ZA 9700824 A	30-10-1998
			US 6020382 A	01-02-2000
			US 5847008 A	08-12-1998
			AU 719663 B2	11-05-2000
			AU 5615298 A	17-07-1998
			CA 2275394 A1	02-07-1998
			EP 0948327 A1	13-10-1999
			JP 2001511767 T	14-08-2001
US 5859051	A	12-01-1999	AT 293963 T	15-05-2005
			AU 1856997 A	22-08-1997
			AU 712607 B2	11-11-1999
			AU 1858197 A	22-08-1997
			CA 2244831 A1	07-08-1997
			DE 69733154 D1	02-06-2005
			EP 1011651 A1	28-06-2000

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/EP2005/001540

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 5859051 A		JP 2000504021 T	04-04-2000
		WO 9728149 A1	07-08-1997
		WO 9727847 A1	07-08-1997
		US 6020382 A	01-02-2000
		US 5847008 A	08-12-1998
		AT 262334 T	15-04-2004
		AU 719146 B2	04-05-2000
		AU 2250797 A	22-08-1997
		CA 2245524 A1	07-08-1997
		DE 69728267 D1	29-04-2004
		DE 69728267 T2	24-02-2005
		EP 0904079 A1	31-03-1999
		ES 2217392 T3	01-11-2004
		JP 2002515865 T	28-05-2002
		WO 9727857 A1	07-08-1997
EP 1284265 A	19-02-2003	JP 2001261674 A	26-09-2001
		EP 1284265 A1	19-02-2003
		US 2003109570 A1	12-06-2003
		WO 0170723 A1	27-09-2001
WO 2004037775 A	06-05-2004	AU 2003273784 A1	13-05-2004
		WO 2004037775 A1	06-05-2004
		US 2005080115 A1	14-04-2005

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

PCT

To:

see form PCT/ISA/220

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY (PCT Rule 43bis.1)

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No.
PCT/EP2005/001540

International filing date (day/month/year)
10.02.2005

Priority date (day/month/year)
12.02.2004

International Patent Classification (IPC) or both national classification and IPC
C07D333/54, C07D333/56, C07D417/12, C07D307/79, C07D307/80, A61K31/343, A61K31/381, A61K31/427,

Applicant
SMITHKLINE BEECHAM CORPORATION

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☒ Box No. II Priority
- ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☒ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☒ Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:



European Patent Office
D-80298 Munich
Tel. +49 89 2399 - 0 Tx: 523656 epmu d
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Authorized Officer

Helps, I

Telephone No. +49 89 2399-8209



Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
 - ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).
2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
 - a. type of material:
 - ☐ a sequence listing
 - ☐ table(s) related to the sequence listing
 - b. format of material:
 - ☐ in written format
 - ☐ in computer readable form
 - c. time of filing/furnishing:
 - ☐ contained in the international application as filed.
 - ☐ filed together with the international application in computer readable form.
 - ☐ furnished subsequently to this Authority for the purposes of search.
3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

Box No. II Priority

1. ☒ The validity of the priority claim has not been considered because the International Searching Authority does not have in its possession a copy of the earlier application whose priority has been claimed or, where required, a translation of that earlier application. This opinion has nevertheless been established on the assumption that the relevant date (Rules 43*bis*.1 and 64.1) is the claimed priority date.
2. ☐ This opinion has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rules 43*bis*.1 and 64.1). Thus for the purposes of this opinion, the international filing date indicated above is considered to be the relevant date.
3. Additional observations, if necessary:

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/EP2005/001540

Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	1-21
	No: Claims	
Inventive step (IS)	Yes: Claims	1-21
	No: Claims	
Industrial applicability (IA)	Yes: Claims	1-19
	No: Claims	20, 21 see below

2. Citations and explanations

see separate sheet

Box No. VI Certain documents cited

1. Certain published documents (Rules 43bis.1 and 70.10)

and / or

2. Non-written disclosures (Rules 43bis.1 and 70.9)

see form 210

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

V. CITATIONS AND EXPLANATIONS

The following documents are mentioned in this Written Opinion

WO-A-97 28149	(A)
US-A-5,859,051	(B)
EP-A-1,284,265	(C)
WO-A-2004 037775	(D)

The novel structural feature of the presently claimed compounds over the intermediate document (D) is the X3 group, which is a bond, alkylene, propylene or methylene bearing a C1-4 alkyl group. The dependent claims 2-15, as well as claim 16 drawn to compounds of claim 1 for use in therapy, claim 17 drawn to pharmaceutical compositions containing compounds of claim 1, claims 18 and 19 drawn to the use of compounds of claim 1 for the manufacture of medicaments, and claims 20-21 drawn to methods of treatment using compounds of claim 1 are novel by consequence. Claims 1 to 21 therefore meet the Novelty requirements of Article 33(2) PCT.

Documents (A) and (B) describe some hPPAR activators based on benzofurans and benzothiophenes which are substituted at the 6 or 7 positions by a phenoxypropoxy or phenylthiopropoxy group, the phenyl being substituted by an acetic acid moiety (see example 11 of (A) and examples 5, 6, 8, 9, 20, 21, and 25-30 of (B)). The presently claimed benzofuran and benzothiophene derivatives have at least two structural differences from the cited compounds of (A) and (B), the benzothiophene or benzofuran is substituted at the 2-position instead of the 6-position, and there is no heteroatom directly linked to the 2-position. Document (C) discloses the compound 3-(5,6-dimethoxybenzothiophen-2-yl)-2-(4-carboxyphenyl)-2-methylpropionic acid as a hPPAR activator, but there are also two structural differences between this compounds and compounds under the scope of the present application (i.e. the carboxy group is directly bound to the phenyl ring and there is an additional carboxy group linked to the alkylene chain bound to the benzothiophene. Having regard to these structural differences, it would not have been obvious for the skilled man to prepare the presently claimed compounds in order to make available further hPPAR activators for the treatment of cardiovascular disorders. Inventive step (Article 33(3) PCT) can be recognised because the problem of making available further hPPAR

activators has been solved in a non obvious manner (see pages 106-8).

For the assessment of the present claims 20 and 21 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

VI. CERTAIN DOCUMENTS CITED

At present no priority document is available. The examination has been carried out assuming that the priority date is validly claimed. If during the subsequent procedure (e.g. EPO examination) the priority date is found to be invalid for some or all of the presently claimed subject matter, the intermediate document (D) may be taken into consideration for the evaluation of Novelty and/or inventive step.

VIII. CERTAIN OBSERVATIONS ON THE INTERNATIONAL APPLICATION.

The definition "hydrolysable ester" is not clear (Article 6 PCT) because this merely defines a desired property for the ester, and the skilled man cannot determine which esters are meant to be included in this definition without carrying out hydrolysis experiments, which is an undue burden.